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EXAMINER	
LAU, JONATHAN S	
ART UNIT	PAPER NUMBER
1623	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,144	BELMANT ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-35* is/are pending in the application.

4a) Of the above claim(s) *27-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-26* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 06 Apr 2009, in which claim 23 is amended to change the scope and breadth of the claim and withdrawn claims 31 and 33 are amended.

This application is the national stage entry of PCT/IB04/04311, filed 02 Dec 2004; and claims benefit of provisional application 60/579,237, filed 15 Jun 2004; and claims benefit of foreign priority document PCT/IB03/06375, filed 02 Dec 2003. This foreign priority document is in English.

Claims 23-35 are pending in the current application. Claims 27-35, drawn to non-elected inventions, are withdrawn. Claims 23-26 are examined on the merits herein.

Response to Amendment

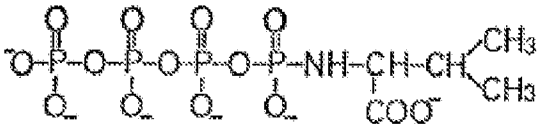
The status of claims 27-35 is withdrawn, pursuant to 37 CFR 1.142(b) as detailed in the Office Action mailed 06 Jan 2009. Applicant's Remarks, filed 06 Apr 2009, acknowledge the status of claims 27-35 as withdrawn from further consideration. However, Applicant's Amendment, filed 06 Apr 2009, does not list the status of claims 27-35 as "withdrawn" or "withdrawn- currently amended".

37 CFR § 1.121(c) provides "In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a

parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered)." 37 CFR § 1.121(c)(2) provides "If a withdrawn claim is currently amended, its status in the claim listing may be identified as "withdrawn- currently amended."

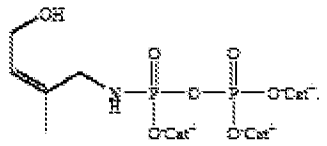
For the purpose of facilitating prosecution Applicant's Amendment, filed 06 Apr 2009, is entered. However, it is reiterated that the status of claims 27-35 is properly withdrawn.

Rejections Withdrawn

Applicant's Amendment, filed 06 Apr 2009, with respect to claims 23, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsuhako et al. (Bull. Chem. Soc. Jpn., 1981, 54, p289-290, of record) has been fully considered and is persuasive, as the compound  does not read upon amended claim 23. Claims 25 and 26 depend from claim 23 and incorporate all limitations therein.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 06 Apr 2009, with respect to claims 23, 25 and 26 are provisionally rejected on the ground of nonstatutory double patenting over claim 31, 32 and 49 of copending Application No. 11/817,450 has been fully considered and is

persuasive, as the compound  does not read upon amended claim 23. Claims 25 and 26 depend from claim 23 and incorporate all limitations therein.

This provisional double patenting rejection has been **withdrawn**.

Claim Objections

Claim 23 is objected to because of the following informalities: Claim 23 appears to recite a composition of matter comprising elements a); b); c); d) wherein element d) comprises a carrier and elements i); ii); iii). As no conjunction is present in the list the composition is implied to comprise each of the elements, however for clarity the list should include a conjunction such as "a composition of matter comprising a); b) and c)." If the elements are recited as alternatives, the list must include a conjunction such as "a composition of matter comprising a); b) or c)."

Appropriate correction is required.

The following are new grounds of rejection not necessitated by Applicant's Amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fox et al. (J. Org. Chem., 2002, 67, p5009-5010, cited in PTO-892) in view of Patini et al. (Chem. Rev. 1996, 96, p3147-3176, cited in PTO-892) and in view of Parvin et al. (Biochemistry, 1969, 8(4), p1748-1755, cited in PTO-892).

Fox et al. discloses the pyrophosphate-containing compound HDMAPP as a metabolic intermediate in the synthesis of IPP for the study of the metabolic process (page 5009, left column, paragraph 1 and right column, figure 1). Fox et al. discloses the pyrophosphate-containing compound HDMAPP in a solvent comprising aqueous ammonium carbonate buffer and isopropanol (page 5010, right column, paragraph 1), which is a pharmaceutically acceptable carrier such as for topical applications.

Fox et al. does not specifically disclose a compound of Formula X or the elected species of NHDMAPP (instant claim 23).

Patini et al. teaches bioisoterism is a well known approach to influence the metabolism of a compound (page 3147, paragraph 1 spanning left column and right column). Patini et al. teaches oxygen and nitrogen are well known isosteres (page 3148, right column, paragraph 2). Patini et al. teaches the monovalent interchange of amino and hydroxyl groups is well known as a classical bioisostere (page 3150, left column, paragraph 3). Patini et al. teaches the oxygen and NH are well known as a classical divalent bioisosteres as well (page 3155, left column, paragraph 2).

Parvin et al. teaches phosphate and phosphoramidate are known in the art of biochemical metabolic studies as substrates of the same enzyme activity (page 1748, abstract), meaning that they are known as bioisosterically equivalent.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Fox et al. in view of Patini et al. and in view of Parvin et al. All of Fox et al., Patini et al. and Parvin et al. are drawn to the study of chemical structure as it relates to metabolism. One of ordinary skill in the art would be motivated to combine Fox et al. in view of Patini et al. and in view of Parvin et al. because Fox et al. teaches HDMAPP for the study of the metabolic process, Patini et al. teaches bioisoterism is a well known approach to influence the metabolism of a compound and Parvin et al. teaches phosphate and phosphoramidate are known in the art of biochemical metabolic studies as bioisosterically equivalent.

Claims 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fox et al. (J. Org. Chem., 2002, 67, p5009-5010, cited in PTO-892) in view of

Patini et al. (Chem. Rev. 1996, 96, p3147-3176, cited in PTO-892) and in view of Parvin et al. (Biochemistry, 1969, 8(4), p1748-1755, cited in PTO-892) as applied to claims 23 and 26 above, and further in view of Sicard et al. (Infection and Immunity, 2000, 68(8), p4375-4377, cited in PTO-892) and Cox et al. (Vaccine, 1997, 15(3), p248-256, cited in PTO-892).

Fox et al. in view of Patini et al. and in view of Parvin et al. teaches as above.

Fox et al. in view of Patini et al. and in view of Parvin et al. does not specifically teach the composition wherein the carrier is an adjuvant (instant claim 24). Fox et al. in view of Patini et al. and in view of Parvin et al. does not specifically teach the composition further comprising an antigen (instant claim 25).

Sicard et al. teaches the one or more of the metabolic intermediates of the pathway disclosed in Fox et al. exhibit immunological stimulatory activity (page 4375, right column, first full paragraph). Sicard et al. teaches IPP produced by the metabolic pathway is also an antigen (page 4376, figure 1 at top of page). Sicard et al. teaches it is desired to increase the immune response of the specific metabolic intermediates (page 4376, left column, paragraph 1).

Cox et al. teaches adjuvants are well known in the art to enhance the immune response of a compound by a number of different modes of action (page 248, paragraph 1 and page 249, table 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Fox et al. in view of Patini et al. and in view of Parvin et al. and further in view of Sicard et al. and Cox et al. All of Fox et al., Patini et al., Parvin et al.

and Sicard et al. are drawn to the study of chemical structure and metabolism. Both of Fox et al. and Sicard et al. are drawn to the metabolic intermediates of the pathway disclosed in Fox et al. One of ordinary skill in the art would be motivated to combine Fox et al. in view of Patini et al. and in view of Parvin et al. and further in view of Sicard et al. because Sicard et al. teaches inherent properties of the compound taught by Fox et al. that are known in the art at the time of the invention. One of ordinary skill in the One of ordinary skill in the art would be motivated to combine Fox et al. in view of Patini et al. and in view of Parvin et al. and further in view of Sicard et al. and Cox et al. because Sicard et al. teaches it is desired to increase the immune response of the specific metabolic intermediates and Cox et al. teaches adjuvants are well known in the art. It would have been obvious to combine the IPP produced by the metabolic pathway that is also an antigen taught by Sicard et al. with the bioisostere of the metabolic intermediate taught by Fox et al. in view of Patini et al. and in view of Parvin et al. to give a composition further comprising an antigen because Sicard et al. teaches they are all antigens for the same purpose. It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted), see MPEP 2144.06 I.

The following modified grounds of rejection are necessitated by Applicant's Amendment, filed 06 Apr 2009, in which claim 23 is amended to change the scope and breadth of the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Amended Claims 23-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 23 recites "Cat+ represents ... organic or mineral cation(s) including proton". Claims 24-26 depend from claim 23 and incorporate all limitations therein. Claim 25 recites "antigen".

The specification discloses chemicals, such as the cations H^+, Na^+, NH_4^+, K^+, Li^+, trimethylamine, lysine, and any other pharmaceutically acceptable cations at page 15, lines 15-16 which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 23-26 are directed to encompass organic or mineral cation(s), which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these cations meet the written description provision of 35 USC § 112, first paragraph, due to lacking chemical structural information for what they are and because cations are highly variant and encompass a myriad of possibilities.

The specification provides insufficient written description to support the genus encompassed by the claim. The specification provides only non-limiting examples of the preferred embodiments, such as the well-defined group of pharmaceutically acceptable cations at page 15, lines 15-16.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The recitation “antigen” is seen to be merely functional language. The terms “antigen” defines a compound solely by its function in an organism, and does not necessarily convey structural information.

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does “little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate”. The CAFC further clearly states that “[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials” at 1405(emphasis added), and that “It does not define any structural features commonly possessed by members of the genus

that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

With the exception of the above specifically disclosed chemical structures, the skilled artisan cannot envision the detailed chemical structure of the encompassed cations or antigens, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly

> conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the structurally defined chemical compounds, but not the full breadth of the claims, meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See Vas-Cath at page 1115.)

The court of *In re Curtis* held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when… the evidence indicates ordinary artisans could not predict the operability … of any other species." (see *In re Curtis* 354 F.3d 1347, 69 USPQ2d 1274, Fed. Cir. 2004). The court of *Noelle v. Lederman* also pointed out that generic claim to anti-CD40CR Mabs lacked written description support because there was no description of anti-human or other species Mabs, and no description of human CD40CR antigen. The court further pointed out that attempt to "define an unknown by its binding affinity to another unknown" failed. See 355 F.3d 1343, 69 USPQ2d 1508, Fed. Cir. 2004.

Response to Applicant's Remarks:

Applicant's Remarks, filed 06 Apr 2009, have been fully considered and found not to be persuasive.

Applicant notes that the term antigen is well defined in the art, and that the general properties of antigens are well known. Applicant provides evidence in the form of a text book establishing this fact. It is noted that the specification at page 17, paragraph 159 defines an preferred embodiment of an antigen. The specification at page 33, lines 25-30 states that the antigen component can be selected from virtually any antigen, antigenic determinant or hapten. Brock (Madigan et al., Brock Biology of Microorganisms, 1997, 8th ed., p813-819, cited in PTO-892) discloses that an antigen is defined as any molecule capable of interacting with specific components of the immune system (page 814). Brock at page 819 discloses that not all antigens are immunogens that induce an immune response and that an enormous variety of macromolecules that are foreign can act as immunogens under appropriate conditions. As recited above, the skilled artisan cannot envision the detailed chemical structure of the encompassed antigens, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The chemical structure itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. That the general properties of antigens are well known does not necessarily translate into the structure of the antigens being well known, as an enormous variety of macromolecules that are foreign can act as immunogens, and therefore antigens, under appropriate conditions. The term

antigen defines a functional property that does not define any structural features commonly possessed by members of the genus that distinguish from others.

Conclusion

No claim is found to be allowable.

This Office Action details new grounds of rejection not necessitated by Applicant's Amendment. Accordingly, this Office Action is Non-Final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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